

CLINICAL PHARMACOLOGY OF ARRHYTHMIAS

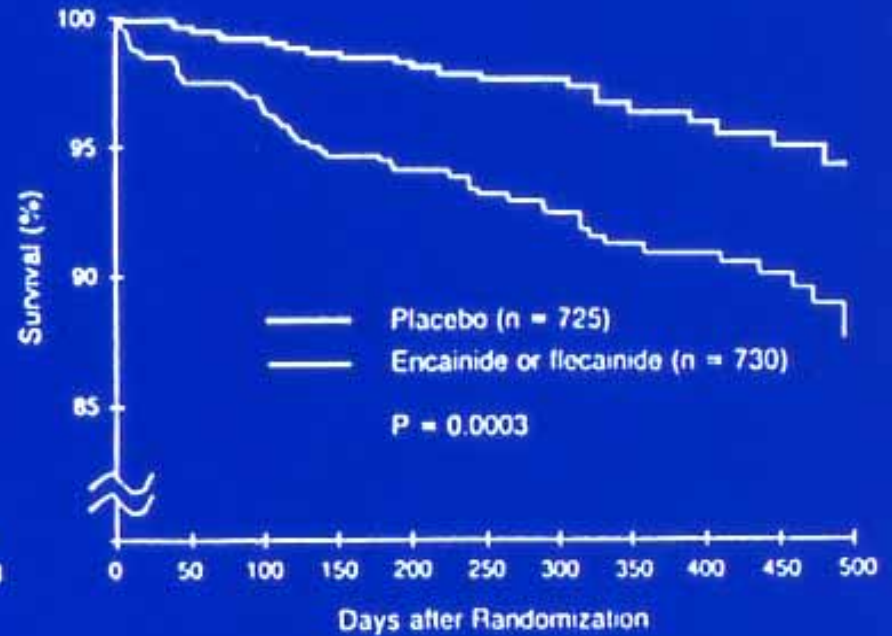
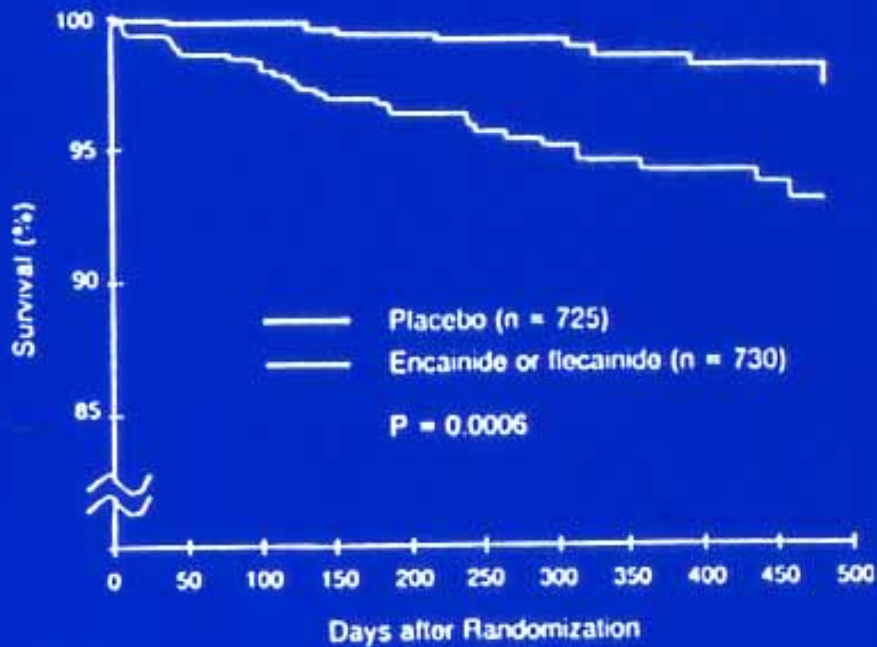
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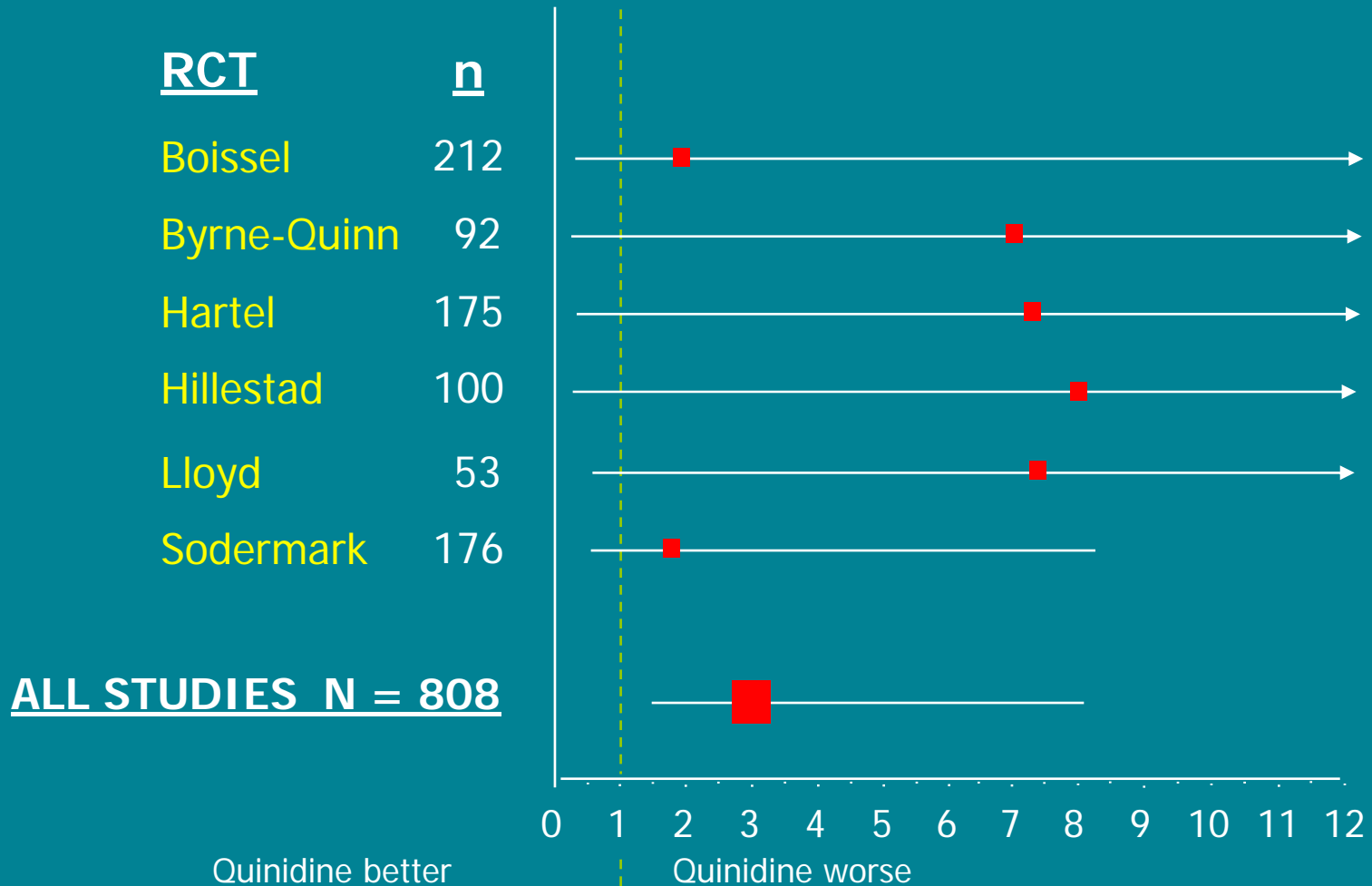
VAUGHAN – WILLIAMS CLASSIFICATION

- **Class I** : sodium inhibitors
 - Ia : Quinidine, Disopyramide
 - Ib : Lidocaïne, Mexiletine
 - Ic : Flecaïnide, Propafenone, Cibenzoline
- **Class II** : beta-blockers
- **Class III** : potassium blockers : Amiodarone, Sotalol
- **Class IV** : calcium inhibitors : Verapamil, Diltiazem



CAST 1989

Odds Ratio/Total mortality of patients treated by quinidine /Control



Odds Ratio (Quinidine: Control)

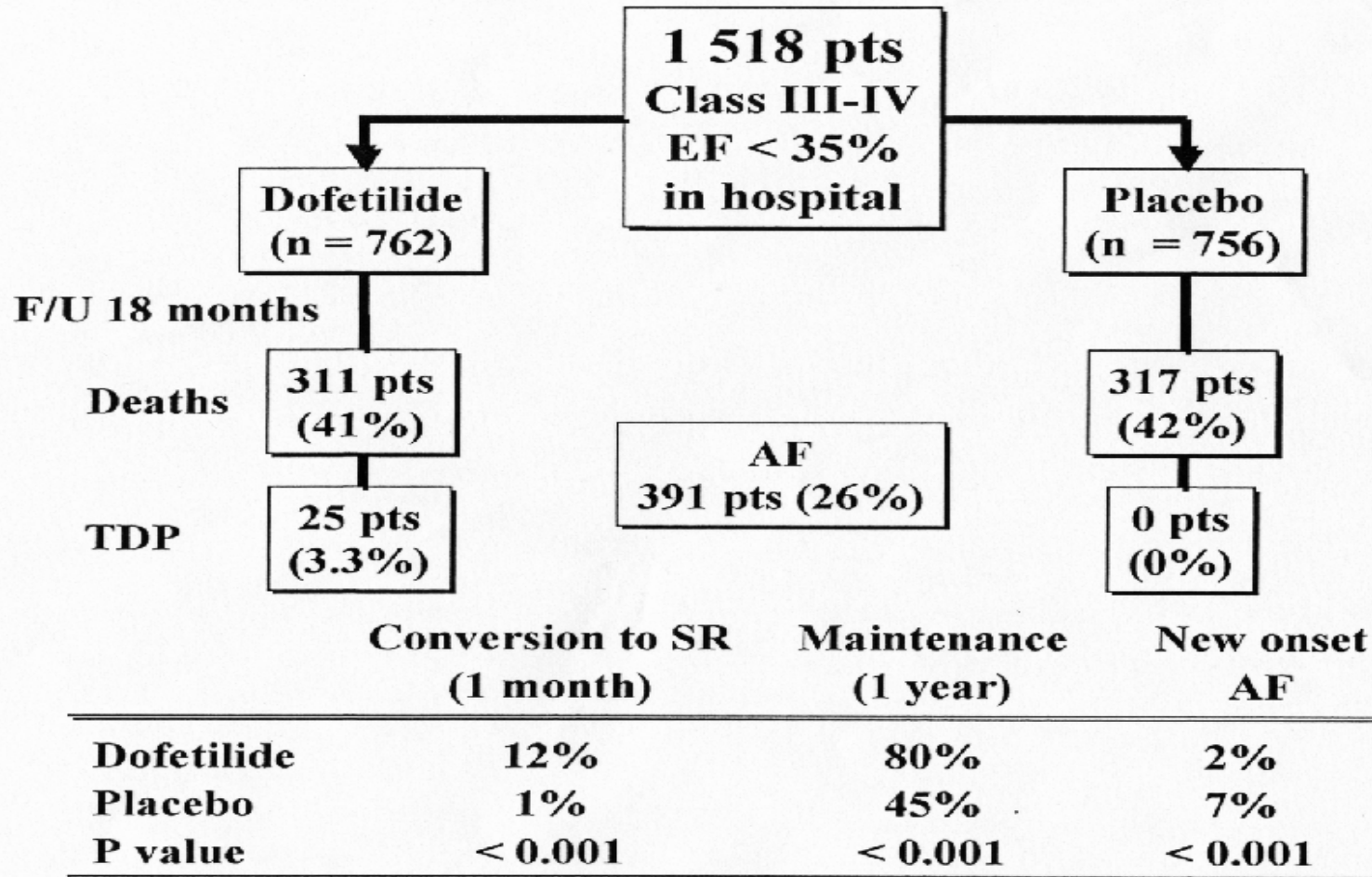
Coplen SE. Circulation. 1990;82:1106-1116.



CLASS III ANTI-ARRHYTHMIC DRUGS

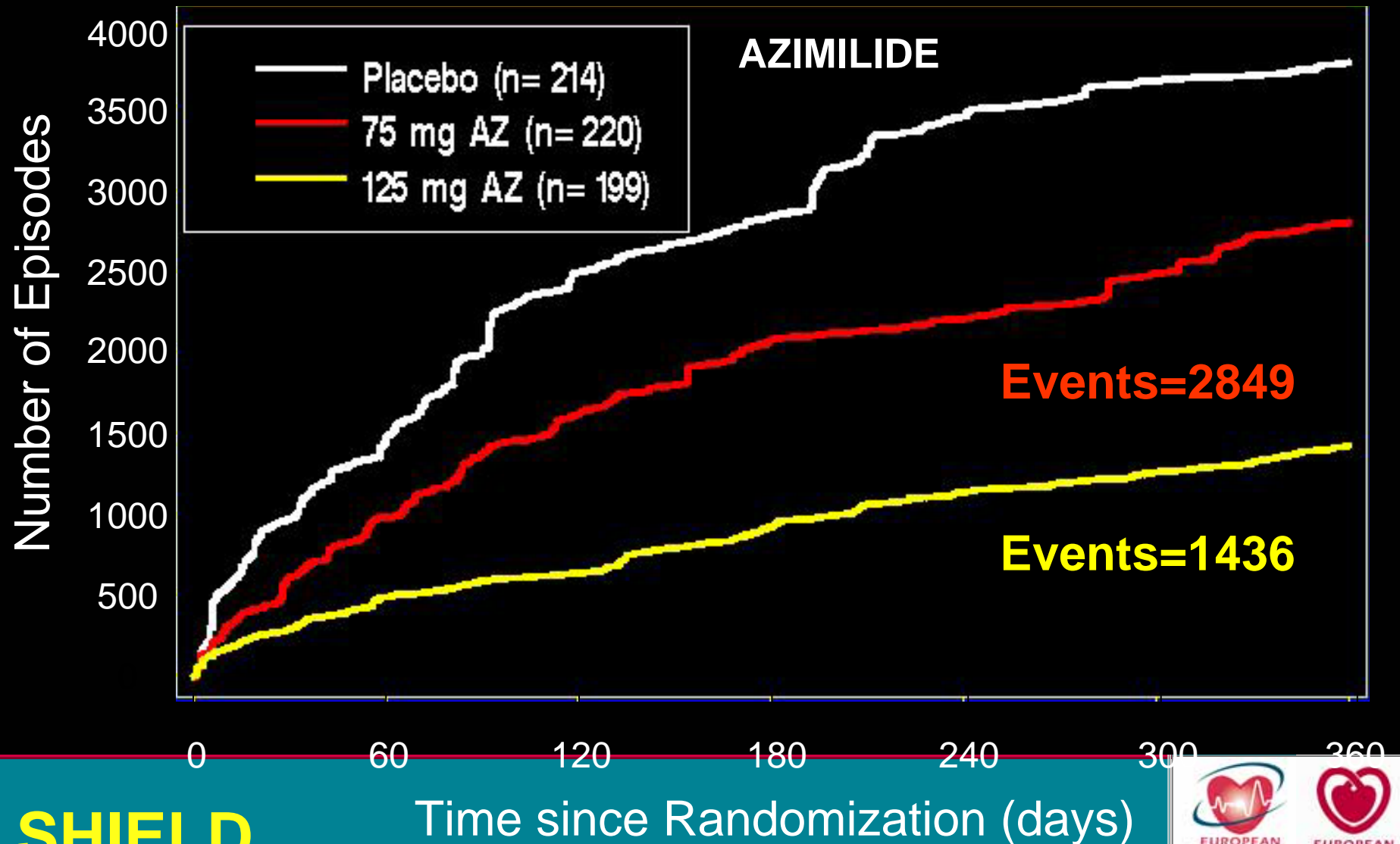
- LY 190417
- Clofilium
- Melperone
- MS 551
- Ambasilide
- Sematilide
- WAY 123,398
- E 4031
- MDL 11,939
- Risotilide
- Acecainide
- Terikalant
- Almokalant
- SB 237376
- Amiodarone
- DL Sotalol
- Tedisamil
- Ibutilide
- Dofetilide
- Azimilide
- Dronedarone
- Celivarone
- Vernakalant

DIAMOND CHF



Torp-Pederson NEJM 1999

Cumulative Episodes of Appropriate (VT/VF) ICD Therapy Episodes



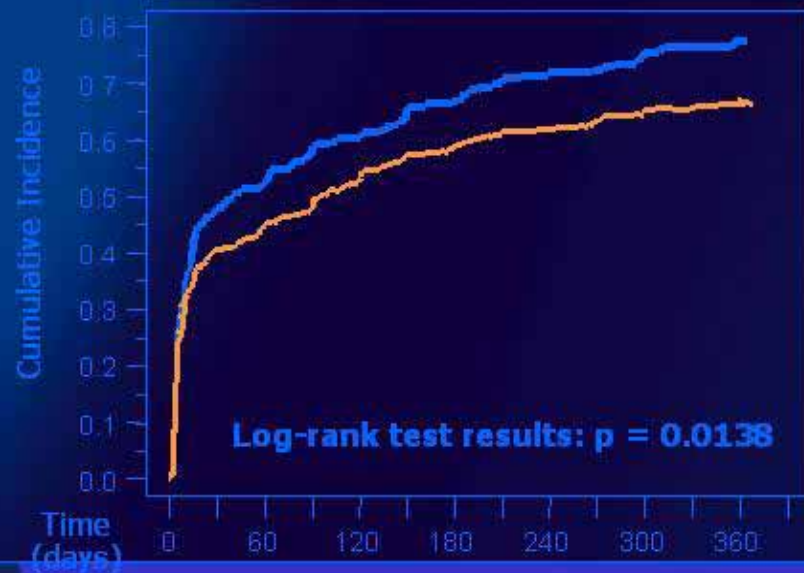
SHIELD

Time since Randomization (days)

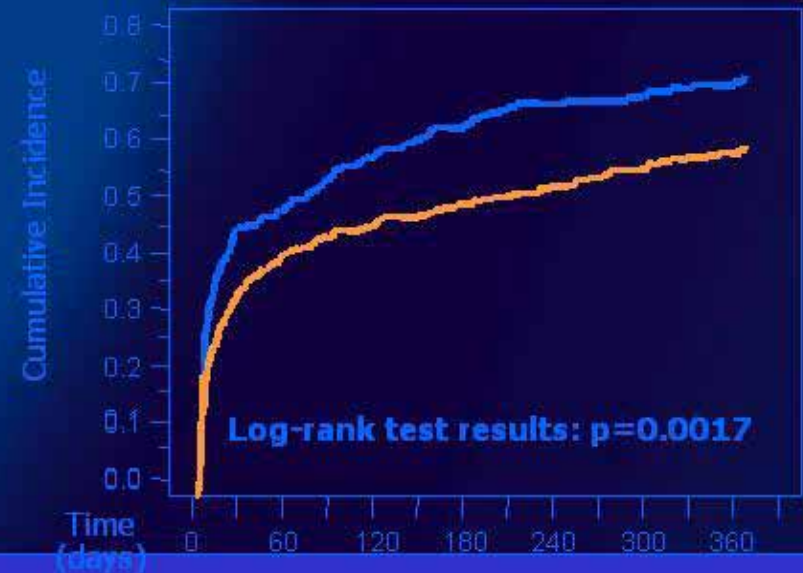


Primary end point : patients with adjudicated first recurrence of AF / A flutter

EURIDIS



ADONIS

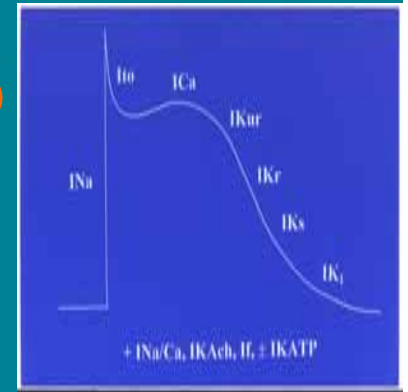


— Placebo — Dronedaron 400 mg bid

DRONEDARONE



ATRIAL REPOLARIZATION DELAYING AGENTS (ARDAs)



Vernakalant (RSD 1235):

- Class III antiarrhythmic drug mainly acting on I_{Kur} (preferential effect on atrium), but also blocking Na^+ channels
- Effective for sinus rhythm restoration by IV route, restores sinus rhythm in 52 % of patients (median time 14 minutes)

Other drugs : AZD7009, AVE0118, S9947/S20951, NP142, Xen-D0101/2

OTHER MODES OF ACTION

▪ Antiarrhythmic agents :

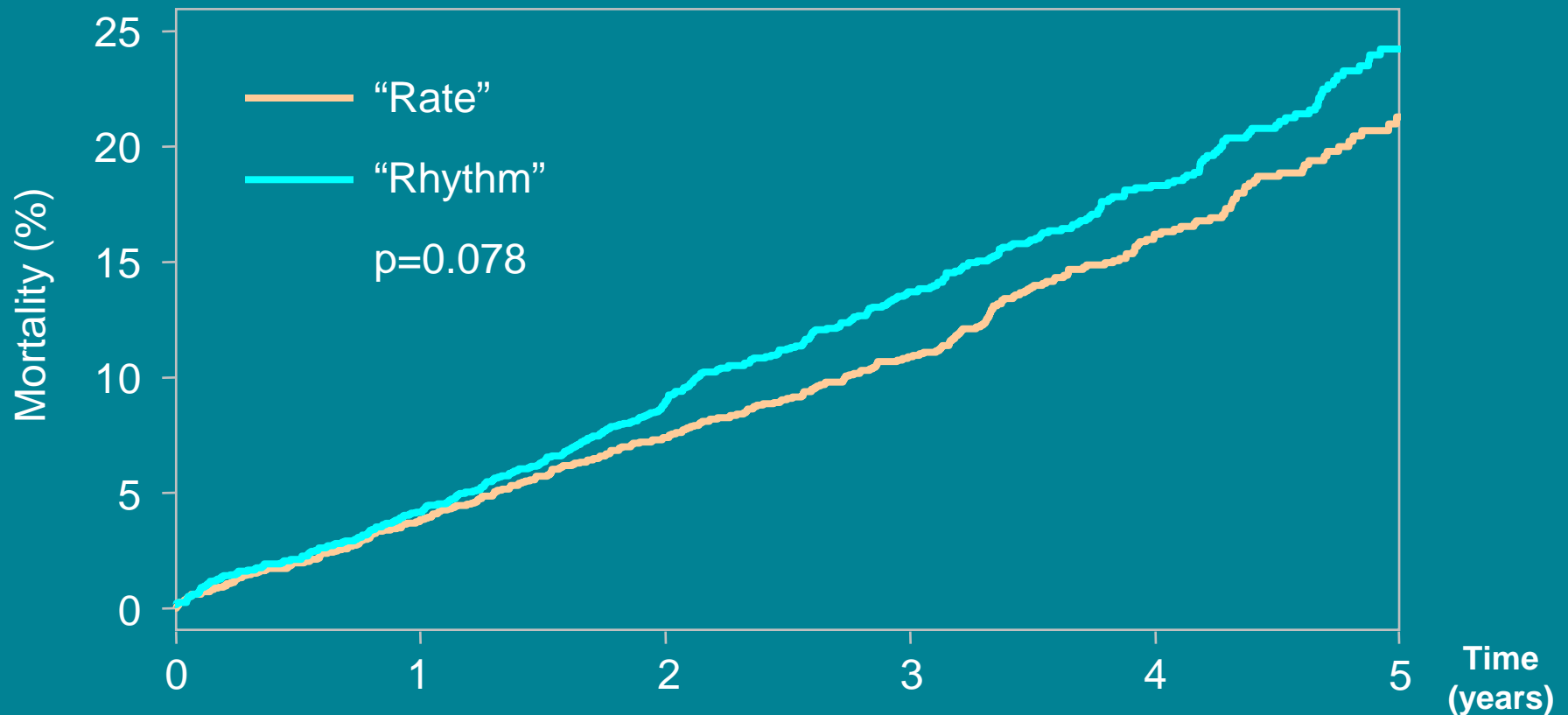
- Na⁺ / H⁺ exchanger inhibitors : Cariporide, Zoniporide, Eniporide, Sabiporide
- Na⁺ / Ca⁺⁺ exchanger inhibitors : KB R7943
- Connexin modulators : AAP 10, GAP 485
- Stretch activated channel inhibitors : GsMx4 (tarantula spider venom)



▪ Rate control drugs :

- Adenosine A1 receptor agonists : Tecadenoson, DT 1009
- If blockers : Ivabradine, YM 758

Main judgement criterion : total mortality (all etiologies)



“Rate” n : 2027,0
“Rhythm” n : 2033,0

1926,78
1932,80

1827,148
1807,175

1329,210
1316,257

774,275
780,314

236,306
255,352

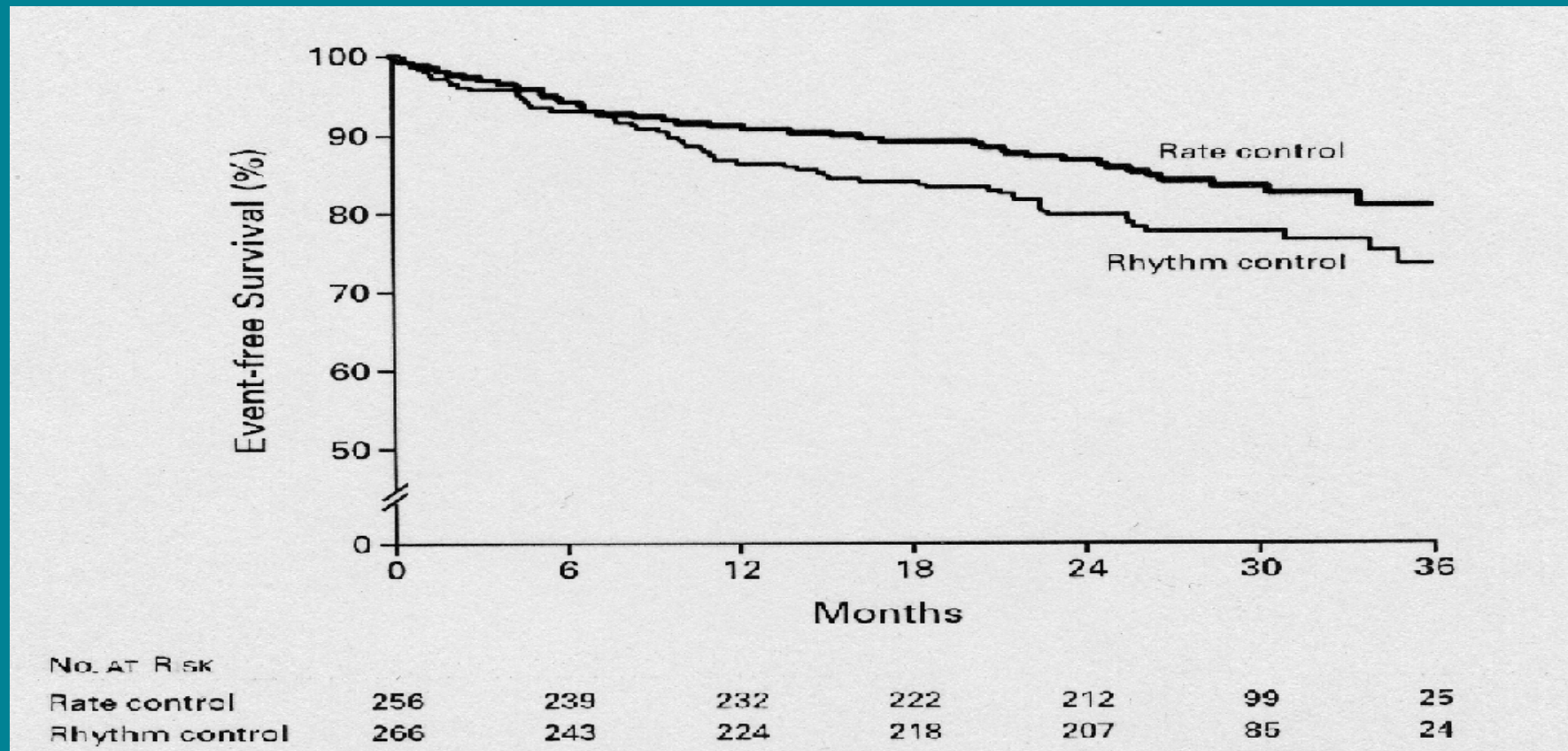


AFFIRM

Atrial Fibrillation Follow-up Investigation of Rhythm Management



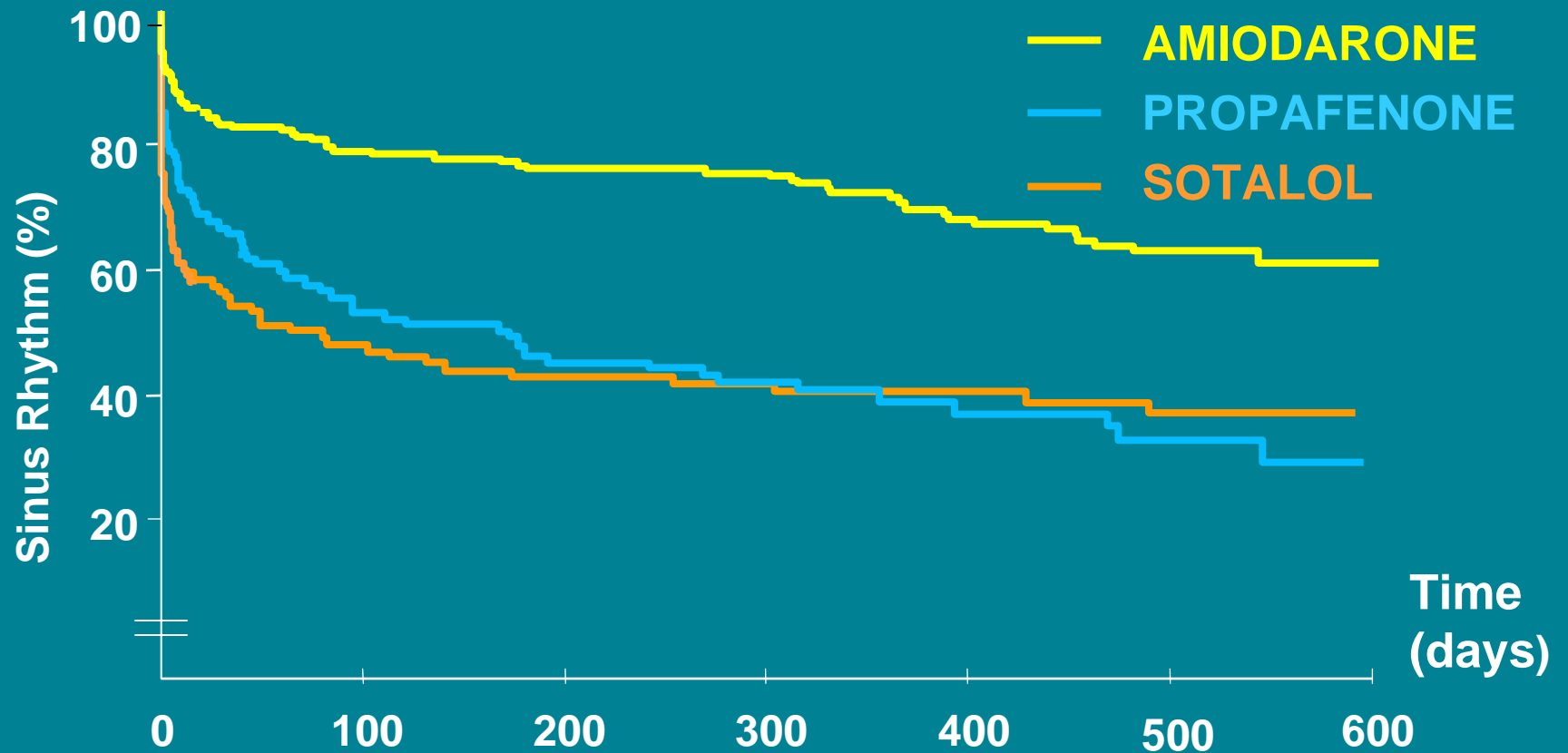
RACE : composite end point (cardiovascular mortality + thromboembolic complications + bleeding + implantation of a pacemaker + heart failure + severe adverse events of antiarrhythmic drugs)



I. Van Gelder et al., N. Engl. J. Med, 2002; 347 : 1834-40



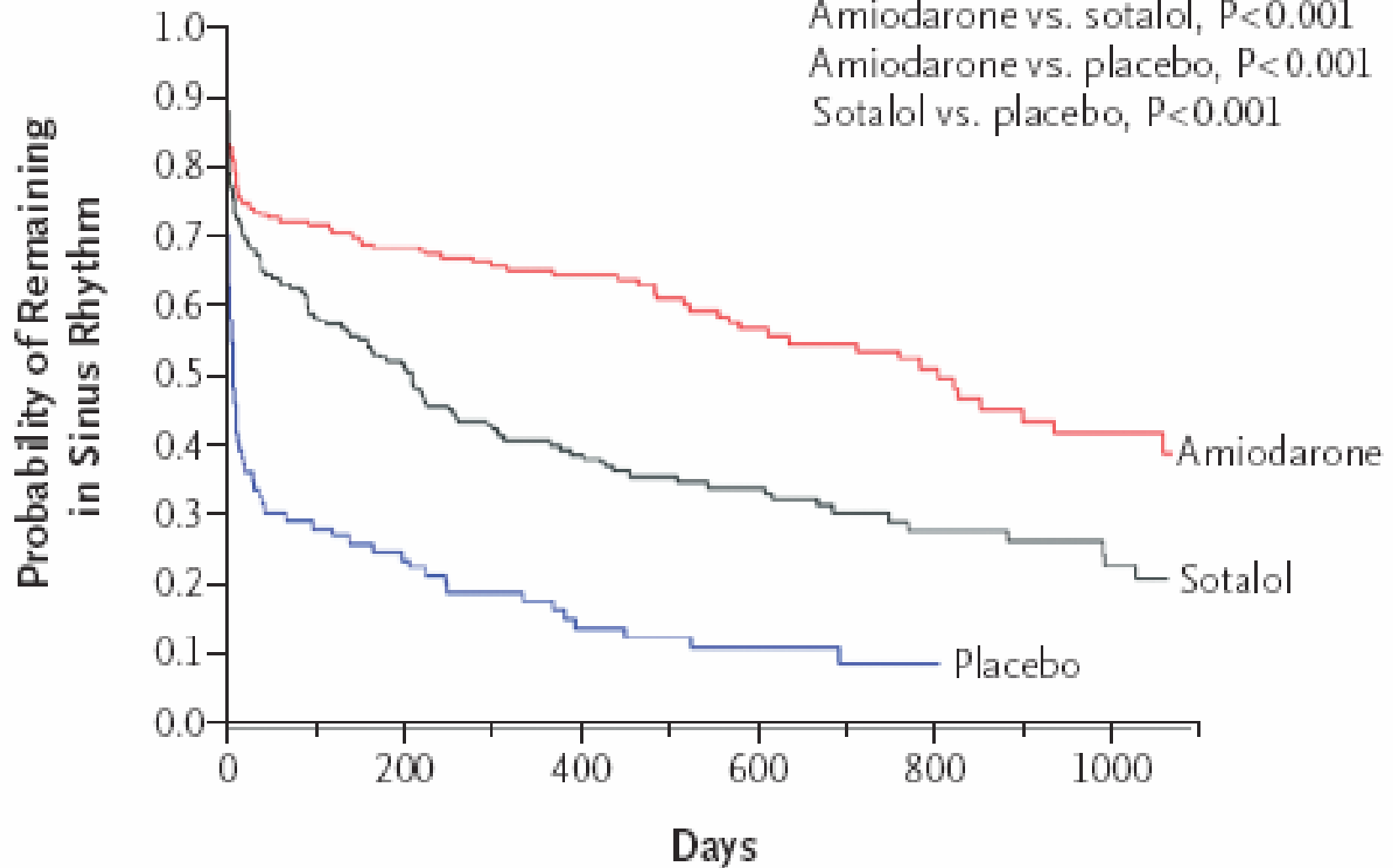
CANADIAN TRIAL OF AF (CTAF)



D. Roy et al. NEJM 2000; 342 : 913-20



SAFE - T



B.N. Singh et al., NEJM 2005 ; 352 : 1861 - 72

2006

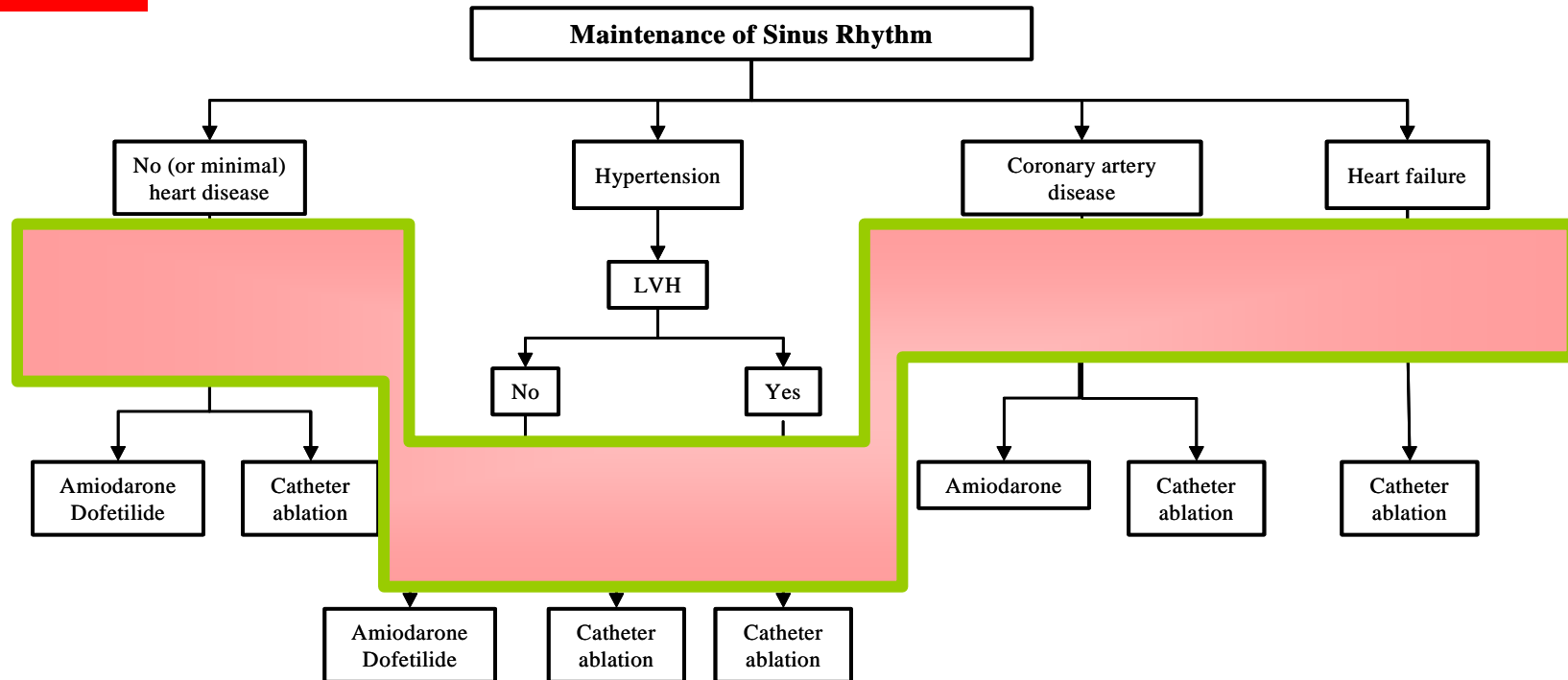


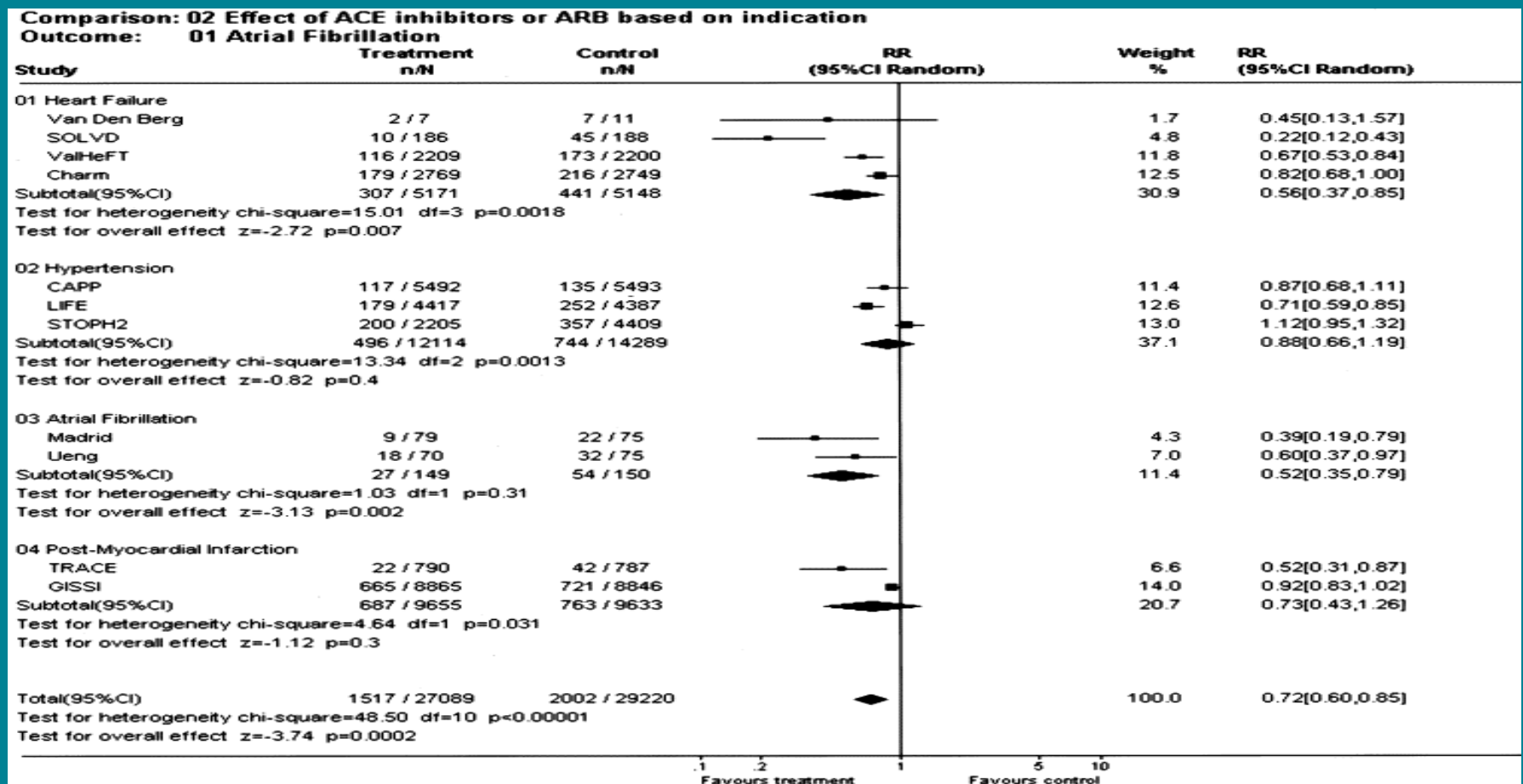
Figure 15. Antiarrhythmic drug therapy to maintain sinus rhythm in patients with recurrent paroxysmal or persistent atrial fibrillation. Drugs are listed alphabetically and not in order of suggested use. The seriousness of heart disease proceeds from left to right, and selection of therapy in patients with multiple conditions depends on the most serious condition present. LVH indicates left ventricular hypertrophy.

NON ANTIARRHYTHMIC DRUGS AND ATRIAL FIBRILLATION

- **Renin Angiotensin Aldosterone System blockers :**
 - Angiotensin Converting Enzyme Inhibitors
 - Angiotensin II Receptor Blockers
 - Antialdosterone
- **Statins,** polyunsaturated fatty acids, steroids, antioxidants...

—————→ **Prevention** of atrial fibrillation and / or prevention of cardiovascular events in patients with atrial fibrillation

PREVENTION OF ATRIAL FIBRILLATION WITH ANGIOTENSIN CONVERTING ENZYME INHIBITORS AND ANGIOTENSIN RECEPTOR BLOCKERS : A METAANALYSIS



Healey J. et al., J. Am. Coll. Cardiol. 2005 ; 45 : 1832 - 9

